Published in final edited form as:

Urology. 2010 November ; 76(5): 1218–1223. doi:10.1016/j.urology.2010.01.066.

Association of Cigarette Smoking With Interval to Biochemical Recurrence After Radical Prostatectomy: Results from the SEARCH Database

Daniel M. Moreira, Jodi A. Antonelli, Joseph C. Presti Jr., William J. Aronson, Martha K. Terris, Christopher J. Kane, Christopher L. Amling, and Stephen J. Freedland

Division of Urologic Surgery, Department of Surgery and Duke Prostate Center and Department of Pathology, Duke University School of Medicine, Durham, North Carolina; Urology Section, Veterans Affairs Medical Center, Durham, North Carolina; Department of Urology, Stanford University Medical Center, Stanford, California; Urology Section, Department of Surgery, Veterans Affairs Medical Center, Palo Alto, California; Urology Section, Department of Surgery, Veterans Affairs Medical Center, Greater Los Angeles, Los Angeles, California; Department of Urology, University of California, Los Angeles, Medical Center, Los Angeles, California; Urology Section, Division of Surgery, Veterans Affairs Medical Center, Augusta, Georgia; Division of Urologic Surgery, Department of Surgery, Medical College of Georgia, Augusta, Georgia; Division of Urology, Department of Surgery, University of California, San Diego, Medical Center, San Diego, California; and Division of Urology, Department of Surgery, Oregon Health and Science University, Portland, Oregon

Abstract

OBJECTIVES—To analyze the association between cigarette smoking and biochemical recurrence (BCR) after radical prostatectomy among men from the Shared Equal Access Regional Cancer Hospital (SEARCH) cohort.

METHODS—We performed a retrospective analysis of 1267 subjects from the SEARCH cohort treated from 1998 to 2008 with smoking status available from the preoperative notes. A comparison of the baseline patient and disease characteristics between the current smokers and nonsmokers (past and never smokers combined) was performed using the chi-square and rank sum tests. The univariate and multivariate associations between smoking status and BCR-free survival were analyzed using Kaplan-Meier plots, the log-rank test, and Cox proportional hazard models.

RESULTS—Of the 1267 patients, 408 (32%) were active smokers and 859 (68%) were nonsmokers at surgery. The current smokers were younger ($P < .001$), more likely to be black ($P < .001$), and had a lower body mass index ($P < .001$), a greater percentage of positive biopsy cores ($P = .039$), a greater preoperative prostate-specific antigen level ($P = .003$), more extracapsular extension ($P = .003$) and seminal vesicle invasion ($P = .029$), and lower prostate volumes ($P = .002$). On univariate analysis, smokers had a risk of BCR similar to that of nonsmokers (hazard ratio 1.19, $P = .129$). On multivariate analysis, smoking was associated with an increased risk of BCR when adjusted for body mass index only (hazard ratio 1.37, $P = .008$). However, after adjustment for multiple preoperative characteristics, the association was attenuated and no longer statistically significant (hazard ratio 1.12, $P = .325$). After additional adjustment for postoperative

features, such as tumor grade and stage, smoking was unrelated to the risk of BCR (hazard ratio 0.91, $P = .502$).

CONCLUSIONS—Among patients undergoing radical prostatectomy in the SEARCH cohort, cigarette smoking was associated with slightly more advanced disease but a similar risk of BCR.

Cigarette smoking is the leading cause of preventable morbidity and mortality in the United States.¹ It has traditionally been associated with an increased incidence of several cancers. Smoking has also been correlated with an increased risk of cancer relapse after treatment and progression to disseminated disease.² However, the association between cigarette smoking and prostate cancer remains unclear. A recent meta-analysis found cigarette smoking was not an important risk factor for prostate cancer incidence.³ However, in that study, the smokers who developed prostate cancer had a worse prognosis and greater prostate cancer-specific mortality, suggesting that smoking could be associated with more aggressive disease or a suboptimal response to cancer therapy. Two studies reported greater prostate cancer progression rates after radiotherapy for localized tumor.^{4,5} However, to date, the effects of smoking on the response to radical prostatectomy have not been evaluated. Therefore, we sought to analyze the association between cigarette smoking and the interval to biochemical recurrence (BCR) after radical prostatectomy among men from the Shared Equal Access Regional Cancer Hospital (SEARCH) database.

MATERIAL AND METHODS

Study Population

After obtaining institutional review board approval from each institution, the data from patients undergoing radical prostatectomy from 1998 to 2008 at 4 Veteran Affairs Medical Centers (West Los Angeles, CA, Palo Alto, CA, Augusta, GA, and Durham, NC) were combined into the SEARCH database.⁶ The database included information on patient age at surgery, race, height, weight, clinical stage, cancer grade on diagnostic biopsies, preoperative prostate-specific antigen (PSA) level, surgical specimen pathologic findings (ie, specimen weight, tumor grade, stage, and surgical margin status), and follow-up PSA level.⁷ The patients treated with preoperative hormonal therapy or radiotherapy were excluded from the present study. Of the 1511 patients in the SEARCH cohort, we excluded 189 (12%) because of missing smoking status at surgery and 55 (4%) because of missing follow-up data, for a study population of 1267 subjects. Smoking status was determined by retrospective chart review of the preoperative surgical and anesthesia notes. We obtained data on cigarette smoking status at surgery (yes/no) and a history of smoking (yes/no). Other types of smoking such as cigars or pipes were not analyzed. Other forms of tobacco exposure such as second-hand smoking or tobacco chewing also were not evaluated in the present study. All patients were followed up with serial PSA determinations and clinical visits at intervals according to the attending physician's discretion. BCR was defined as a single PSA level >0.2 ng/mL, 2 concentrations at 0.2 ng/mL, or secondary treatment for an elevated PSA level.⁸ Additional treatment after surgery was at the judgment of the patient and treating physician.

Statistical Analysis

The patients were divided into 2 groups according to the smoking status at surgery: active smokers and nonsmokers (never and exsmokers). The exsmokers and nonsmokers were combined into 1 group, given previous studies showing such patients have similar risk of prostate cancer mortality and BCR after radiotherapy.^{4,9} Moreover, in exploratory analyses, we found no significant differences in any pathologic or biochemical progression endpoints between the never smokers and exsmokers on either univariate or multivariate analysis, justifying this grouping. Additionally, to explore the possibility that former smokers who

quit more recently had a greater risk than former smokers who had quit a long time before surgery, we used multiple cutpoints of smoking quit date (1, 5, and 10 years before surgery) to separate the men into recent and remote quitting groups. However, regardless of the cutpoint chosen, those who had quit more recently and more remotely had a similar risk of BCR. Moreover, using the interval from quitting smoking to surgery as a continuous variable did not predict for BCR.

A comparison of the baseline characteristics between smokers and nonsmokers was performed using the chi-square test for categorical data and the rank sum test for continuous variables. We also tested whether smoking was independently associated with the binary adverse pathologic features of positive surgical margins, extracapsular extension, and seminal vesicle invasion using a multivariate logistic regression analysis. In these analyses, we mutually adjusted for the preoperative clinical characteristics of patient race (white, black, other), body mass index (BMI, continuous, log-transformed), age at surgery (continuous), year of surgery (continuous), surgical center (1-4), preoperative PSA level (continuous, log-transformed), and biopsy Gleason score (2-6, 3 + 4, and 4 + 3-10). Univariate BCR-free survival analysis was performed using Kaplan-Meier plots and log-rank tests. To test whether smoking was independently predictive of BCR, we used a Cox proportional hazards model, adjusting for the preoperative clinical characteristics, as stated. To assess whether the association between smoking and recurrence was independent of the pathologic findings, we also performed a separate multivariate analysis in which we further adjusted for positive surgical margins, seminal vesicle invasion, extracapsular extension, pathologic Gleason score (2-6, 3 + 4, and 4 + 3-10), and prostate weight (continuous, log-transformed). The proportional hazards assumption was addressed by examining the Schoenfeld residuals of each variable and tested using Grambsch and Therneau's statistic.¹⁰ All statistical analyses were performed using Stata, version 10.0 (StataCorp, College Station, TX), and R2.9.0 (R Foundation for Statistical Computing, Vienna, Austria), with Design, version 2.2-0 and Hmisc, version 3.6-0, libraries. $P < .05$ was considered statistically significant.

RESULTS

Of the 1267 men included in the present study, 408 (32%) were active smokers and 859 (69%) were non-smokers at surgery (Table 1). Overall, the current smokers were significantly younger ($P < .001$) and more likely to be black than were the nonsmokers ($P < .001$). The smokers also had a significantly lower BMI ($P < .001$), greater percentage of positive biopsy cores ($P = .039$), greater preoperative PSA level ($P = .003$), a greater risk of extracapsular extension ($P = .003$) and seminal vesicle invasion ($P = .029$), and lower prostate volumes ($P = .002$). A trend was seen toward an increased risk of positive surgical margins among smokers; however, it did not reach statistical significance (Table 1). Given the association between smoking and adverse pathologic findings, we sought to further explore the correlation between smoking and more advanced disease on multivariate analysis. After adjusting for multiple preoperative features, smoking was independently associated with extracapsular extension (odds ratio 1.61, 95% confidence interval [CI] 1.16–2.25, $P = .005$) but not seminal vesicle invasion (odds ratio 1.30, 95% CI 0.793–2.14, $P = .296$) nor positive surgical margins (odds ratio 1.07, 95% CI 0.81–1.40, $P = .644$).

During a median follow-up of 37 months, the smokers had a risk of developing BCR similar to that of nonsmokers (hazard ratio 1.19, 95% CI .95–1.49, $P = .129$; Fig. 1). Given that we previously found a lower BMI associated with decreased recurrence in this population¹¹ and given that smokers had a lower BMI, we evaluated to what degree this potentially attenuated an association between smoking and recurrence. When the results were adjusted for BMI only, smoking was associated with a significantly increased risk of BCR (hazard ratio 1.37,

95% CI 1.09–2.08, $P = .008$). Furthermore, after stratifying by obesity, we found that obese smokers had a greater risk of BCR compared with obese nonsmokers ($P = .010$; Fig. 2). Among nonobese men, smoking was not associated with the risk of BCR ($P = .257$).

After adjusting for multiple preoperative characteristics, no association was found between smoking and the risk of BCR (hazard ratio 1.12, 95% CI 0.89–1.44, $P = .325$). After the addition of postoperative findings such as surgical margins status, extracapsular extension, seminal vesicle invasion, and pathologic Gleason score, again, no significant association was found between smoking and the interval to BCR (Table 2).

COMMENT

Recent studies have suggested that active smokers are more likely to die of prostate cancer than are nonsmokers.^{3,9,12,13} The greater mortality among smokers could be explained in part by a greater incidence of aggressive disease in active smokers.^{3,12} Alternatively, smoking could be responsible for a suboptimal response to treatment. Two studies of patients with prostate cancer who underwent radiotherapy showed a worse outcome among smokers, even after adjustment for disease aggressiveness.^{4,5} However, the effects of smoking on outcomes in patients who underwent radical prostatectomy have not been evaluated. Therefore, we analyzed the risk of BCR between smokers and nonsmokers among subjects from the SEARCH cohort.

In the SEARCH database, we found the prevalence of active cigarette smoking at surgery to be nearly one third, greater than the approximately 25% prevalence in the general adult male population.¹⁴ In contrast, in a cohort of men undergoing radical prostatectomy at Johns Hopkins, the prevalence of smoking was 5%.¹⁵ It is likely the observed high prevalence of smoking in the present study, especially for a surgical cohort, was related to the high overall prevalence of smoking among Veterans Affairs patients.¹⁶ Moreover, the smokers were younger than the nonsmokers. This finding is supported by population-level studies that found the prevalence of smoking to decrease with age after the fourth decade of life.¹⁷ We also observed active smokers had a significantly lower BMI at surgery, and the prevalence of smoking was lower in obese men. Several studies showed smoking was associated with a lower weight and that smoking cessation can lead to weight gain.^{17,18} Nicotine's physiologic effects result in appetite suppression, increased resting metabolic rates, and reduced calorie storage, which act synergistically to reduce body weight.¹⁸ In agreement with the observations from our surgical cohort, on the population level, smokers also tend to be younger and weigh less.^{14,18}

In our study, smokers had a significantly greater pre-operative PSA level, greater percentage of positive biopsy cores, and greater prevalence of extracapsular extension and seminal vesicle invasion, suggesting that smoking might be associated with more advanced disease at diagnosis. Roberts et al¹⁵ found an association between cigarette smoking and extraprostatic tumor extension among younger men undergoing radical prostatectomy. Additionally, 2 recent meta-analyses of observational studies found smoking was not an important risk factor for prostate cancer incidence but that smokers with prostate cancer tended to have greater mortality from the disease.^{3,12} Although smokers seemed to have more advanced disease than nonsmokers at presentation in the present study, the risk of BCR among smokers was statistically similar to that of the nonsmokers. When adjusted for BMI only, smoking was associated with a greater risk of BCR. In addition, obese smokers had a greater risk of recurrence than did obese nonsmokers. However, smoking did not increase the risk of BCR among nonobese men. Thus, a suggestion was found that the combination of obesity and smoking could result in a particularly aggressive cancer. Whether this resulted from shared biologic causes or was a function of selection bias (ie,

obese smokers might have been discouraged from undergoing surgery unless they had more aggressive disease) or some other reason is unknown, and more study is needed to confirm these findings and to explore the possible reasons.

After adjustment for patient characteristics, tumor grade, and tumor stage, the effect of smoking on BCR was essentially null. Two studies considered the association of smoking and outcomes in patients with prostate cancer treated with radiotherapy. The first study found that smokers had a slightly greater risk of BCR.⁴ In the second study, smoking was shown to be associated with a greater progression to metastatic disease.⁵ These findings suggest that smoking might play a role in cancer progression after radiotherapy but not surgery. One possible explanation for this disparity in outcomes between radical prostatectomy and radiotherapy might relate to smoking-induced tissue hypoxia.¹⁹ Given that radiotherapy requires oxygenated tissue to enact cell killing, it is possible that smoking results in intratumor hypoxia, which would, in theory, explain why smokers treated with radiotherapy have poorer outcomes than nonsmokers. In contrast, the effectiveness of surgery would be unrelated to tissue hypoxia, because surgery relies on complete malignancy excision, regardless of intratumor perfusion. Ultimately, if this dichotomy between outcomes after radiotherapy and surgery is confirmed in future studies, it would suggest that surgery might be the preferable oncologic treatment relative to radiotherapy for active smokers with localized prostate cancer, notwithstanding the potential surgical complications related to surgery in men with greater smoking-related comorbidities. Nevertheless, additional studies are required to establish the association between smoking and BCR after radical prostatectomy.

Given the data to link smoking with prostate cancer progression and death, it was noteworthy that several plausible biologic mechanisms could explain how smoking can accelerate the course of prostate cancer. For example, smoking has an antiestrogen effect that, in turn, might promote prostate cancer growth.²⁰ In addition, smoking is associated with a myriad of genetic and epigenetic abnormalities, such as gene mutations, deletions, and DNA methylation. For instance, the polycyclic aromatic hydrocarbons present in tobacco smoke can induce mutations in the p53 gene, which could potentially lead to worse cancer progression.²¹ Smoking has also been demonstrated to affect the immune system by both promoting inflammation and suppressing the immune function such as reducing T-cell and natural killer cell activation.²² Both pathways (inflammation and decreased immune function) could facilitate tumor growth. Finally, confounder factors might play a role in the association between smoking and aggressive disease. For example, cigarette smoking has been associated with greater ethanol consumption, lower exercise rates, and an overall unhealthy lifestyle.²³ Although, the epidemiologic association between lifestyle characteristics such as exercise and ethanol consumption with prostate cancer progression remains murky, it is likely that a combination of these biologic and behavioral factors is responsible for the association between smoking and aggressive prostate cancer.

The main limitation of our study was the retrospective nature of our cohort. In addition, cigarette smoking has generally been associated with comorbidities such as cardiovascular disease, which were not controlled in our analyses. These comorbidities might, in turn, influence the decision of whether a patient should undergo radical prostatectomy. For example, patients at greater surgical risk with less-aggressive disease could undergo other treatments (e.g., watchful waiting) and those with similar surgical risk and more aggressive disease could be assigned to surgery. This would result in more aggressive disease in the high comorbidity group (ie, smokers) relative to the low comorbidity group (ie, nonsmokers). However, except for slightly greater preoperative PSA levels in smokers, we did not find any other evidence of more aggressive disease among the smokers in the preoperative variables (ie, greater biopsy Gleason score or greater clinical stage) to support

such a hypothesis. We did not analyze the cumulative and current amount of tobacco exposure, because these data were not available for most of the smokers. We also did not analyze other types of tobacco exposure (eg, cigars or chewing tobacco) or different forms of tobacco exposure, because the number of men in those categories was presumably low. Although earlier BCR has been shown to correlate with greater mortality²⁴ and given cigarette smoking can increase the risk of death by noncancer-related causes, studies analyzing smoking history and long-term outcomes after radical prostatectomy such as mortality and metastasis are needed to further identify the independent effects of smoking on cancer progression. Finally, given our relatively modest follow-up (37 months), additional studies with larger sample sizes and longer follow-up are needed to confirm or refute these findings.

CONCLUSIONS

Among patients undergoing radical prostatectomy, cigarette smoking was associated with younger age, black race, lower BMI, a greater percentage of positive biopsy cores, a greater preoperative PSA level, lower prostate volumes, more extracapsular extension, and greater seminal vesicle invasion. Although smoking was associated with more advanced tumors when stratified by the clinical and pathologic characteristics, the risk of BCR was statistically similar between the smokers and nonsmokers.

Acknowledgments

This study was supported by the Department of Veterans Affairs, National Institute of Health grant R01CA100938 (to W. J. Aronson), National Institutes of Health Specialized Programs of Research Excellence grant P50 CA92131-01A1 (to W. J. Aronson), the Georgia Cancer Coalition (to M. K. Terris), Department of Defense Prostate Cancer Research Program (to S. J. Freedland), and the American Urological Association Foundation/Astellas Rising Star in Urology Award (to S. J. Freedland).

References

1. Danaei G, Ding EL, Mozaffarian D, et al. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. *PLoS Med*. 2009; 6:e1000058. [PubMed: 19399161]
2. Guo NL, Tosun K, Horn K. Impact and interactions between smoking and traditional prognostic factors in lung cancer progression. *Lung Cancer*. 2009; 66:386–392. [PubMed: 19304339]
3. Zu K, Giovannucci E. Smoking and aggressive prostate cancer: a review of the epidemiologic evidence. *Cancer Causes Control*. Epub 2009 June 27.
4. Pickles T, Liu M, Berthelet E, et al. The effect of smoking on outcome following external radiation for localized prostate cancer. *J Urol*. 2004; 171:1543–1546. [PubMed: 15017216]
5. Pantarotto J, Malone S, Dahrouge S, et al. Smoking is associated with worse outcomes in patients with prostate cancer treated by radical radiotherapy. *BJU Int*. 2007; 99:564–569. [PubMed: 17166241]
6. Moreira DM, Banez LL, Presti JC Jr, et al. Predictors of secondary treatment following biochemical recurrence after radical prostatectomy: results from the shared Equal Access regional Cancer Hospital database. *BJU Int*. 2009; 105:28–33. [PubMed: 19522861]
7. Moreira DM, Jayachandran J, Presti JC Jr, et al. Validation of a nomogram to predict disease progression following salvage radio-therapy after radical prostatectomy: results from the SEARCH database. *BJU Int*. 2009; 104:1452–1456. [PubMed: 19466946]
8. Freedland SJ, Sutter ME, Dorey F, et al. Defining the ideal cutpoint for determining PSA recurrence after radical prostatectomy. Prostate-specific antigen. *Urology*. 2003; 61:365–369. [PubMed: 12597949]
9. Gong Z, Agalliu I, Lin DW, et al. Cigarette smoking and prostate cancer-specific mortality following diagnosis in middle-aged men. *Cancer Causes Control*. 2008; 19:25–31. [PubMed: 17906959]

10. Grambsch PM, Therneau TM. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika*. 1994; 81:12.
11. Freedland SJ, Sun L, Kane CJ, et al. Obesity and oncological outcome after radical prostatectomy: impact of prostate-specific antigen-based prostate cancer screening: results from the shared Equal Access regional Cancer Hospital and Duke Prostate center databases. *BJU Int*. 2008; 102:969–974. [PubMed: 18691175]
12. Huncharek M, Haddock S, Reid R, et al. Smoking as a risk factor for prostate cancer: a meta-analysis of 24 prospective cohort studies. *Am J Public Health*. 2009 July 16.
13. Rohrmann S, Genkinger JM, Burke A, et al. Smoking and risk of fatal prostate cancer in a prospective U.S. study. *Urology*. 2007; 69:721–725. [PubMed: 17445658]
14. Centers for Disease Control and Prevention (CDC). Cigarette smoking among adults—United States, 2007. *MMWR Morb Mortal Wkly Rep*. 2008; 57:1221–1226. [PubMed: 19008790]
15. Roberts WW, Platz EA, Walsh PC. Association of cigarette smoking with extraprostatic prostate cancer in young men. *J Urol*. 2003; 169:512–516. [PubMed: 12544299]
16. Klevens RM, Giovino GA, Peddicord JP, et al. The association between veteran status and cigarette-smoking behaviors. *Am J Prev Med*. 1995; 11:245–250. [PubMed: 7495601]
17. Flegal KM. The effects of changes in smoking prevalence on obesity prevalence in the United States. *Am J Public Health*. 2007; 97:1510–1514. [PubMed: 17600266]
18. Yore MM, Fulton JE, Nelson DE, et al. Cigarette smoking status and the association between media use and overweight and obesity. *Am J Epidemiol*. 2007; 166:795–802. [PubMed: 17607016]
19. Jensen JA, Goodson WH, Hopf HW, et al. Cigarette smoking decreases tissue oxygen. *Arch Surg*. 1991; 126:1131–1134. [PubMed: 1929845]
20. Hickey K, Do KA, Green A. Smoking and prostate cancer. *Epidemiol Rev*. 2001; 23:115–125. [PubMed: 11588835]
21. Kudahetti S, Fisher G, Ambroisine L, et al. p53 Immunohistochemistry is an independent prognostic marker for outcome in conservatively treated prostate cancer. *BJU Int*. 2009; 104:20–24. [PubMed: 19239456]
22. Mehta H, Nazzari K, Sadikot RT. Cigarette smoking and innate immunity. *Inflamm Res*. 2008; 57:497–503. [PubMed: 19109742]
23. Ferrucci L, Izmirlian G, Leveille S, et al. Smoking, physical activity, and active life expectancy. *Am J Epidemiol*. 1999; 149:645–653. [PubMed: 10192312]
24. Freedland SJ, Humphreys EB, Mangold LA, et al. Time to prostate specific antigen recurrence after radical prostatectomy and risk of prostate cancer specific mortality. *J Urol*. 2006; 176:1404–1408. [PubMed: 16952644]

Figure 1.
 BCR-free survival after radical prostatectomy in SEARCH cohort stratified by smoking status at surgery.

Figure 2.
BCR-free survival after radical prostatectomy in SEARCH cohort stratified by obesity and smoking status at surgery.

Table 1

Baseline characteristics

Variable	Smokers (n)	Nonsmokers (n)	P Value
Total patients (n)	408 (32)	859 (68)	—
Age at surgery (y)			<.001
Median	59	61	
Interquartile range	55–63	58–65	
Ethnic group			<.001
White	187 (46)	453 (53)	
Black	203 (50)	338 (40)	
Other	18 (4)	64 (7)	
Body mass index (kg/m ²)			<.001
Median	26.9	28.5	
Interquartile range	23.6–29.4	26.2–32.0	
Year of surgery			.068
Median	2004	2004	
Interquartile range	2002–2006	2002–2006	
Clinical stage			.111
T1	250 (64)	554 (68)	
T2–T3	142 (36)	256 (32)	
Biopsy Gleason score			.363
2–6	226 (55)	505 (59)	
3 + 4	100 (25)	198 (23)	
≥4 + 3	82 (20)	148 (17)	
Positive biopsy core (%)			.039
Median	33	30	
Interquartile range	16–50	16–50	
Preoperative PSA (ng/mL)			.003
Median	6.7	6.2	
Interquartile range	4.8–10.8	4.5–8.9	
Postoperative Gleason score			.149
2–6	144 (35)	353 (41)	
3 + 4	178 (44)	338 (39)	
≥4 + 3	84 (21)	167 (20)	
Extracapsular extension	101 (25)	153 (18)	.003
Positive surgical margins	181 (45)	349 (41)	.200
Seminal vesicle invasion	39 (10)	53 (6)	.029
Lymph node status			.518*
Positive	7 (2)	10 (1)	
Negative	292 (72)	575 (67)	
Not sampled	109 (26)	274 (32)	
Prostate weight (g)			.002

Variable	Smokers (n)	Nonsmokers (n)	P Value
Median	38	40	
Interquartile range	30–49	32–52	

* Patients with unknown lymph node status excluded from present analysis.

Table 2

Postoperative predictors of biochemical recurrence

Variable *	HR	95% CI	P Value
Smoking	0.91	0.70–1.18	.502
Year of surgery	0.99	0.95–1.04	.823
Age at surgery (y)	1.02	1.00–1.04	.037
Ethnic group			
White	Referent	—	—
Black	1.31	1.03–1.68	.030
Other	1.11	0.64–1.91	.712
Body mass index (log[kg/m ²])	4.49	2.09–9.65	<.001
Preoperative PSA (log[ng/mL])	1.57	1.30–1.91	<.001
Pathologic Gleason score			
2–6	Referent	—	—
3 + 4	2.17	1.53–3.09	<.001
≥4 + 3	3.94	2.71–5.72	<.001
Extracapsular extension	1.23	0.92–1.63	.159
Positive surgical margins	1.81	1.40–2.33	<.001
Seminal vesicle invasion	2.44	1.74–3.43	<.001
Prostate weight (log[g])	0.47	0.34–0.64	<.001

HR = hazard ratio; CI = confidence interval.

* Adjusted for Veterans Affairs Medical Center.